REMARKS

The Official Action dated December 17, 2002 has been carefully considered. It is believed that the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

The specification has been amended on page 1 in order to reflect the status of USSN 09/442,143. We do not understand the requirement to list the relationship between the present application and USSN 09/442,143 as the relationship was indicated in the Preliminary Amendment that was filed on July 11, 2001.

We also do not understand the statement that the "limitation which includes treating graft rejection does not have support in the parent application 09/442,143". We point out that the disclosure of the present application is **identical** to the parent application and that no new matter has been added. Consequently, the present application is correctly a divisional of the parent application. Both the present application and the parent application clearly does teach the treatment of graft rejection as an aspect of the invention, for example on page 6, lines 6-10.

35 USC §112

1. Enablement

The Examiner has objected to claims 1-4 under 35 USC §112, first paragraph alleging that the specification is only enabling for a method of preventing or treating intestinal transplants and xenogeneic hyperacute liver failure comprising administering an antibody to SEQ ID NO:2 or SEQ ID NO:18. We respectfully disagree with the Examiner for the reasons that follow.

Applicant is duly entitled to claims for a method of preventing or treating any graft rejection using any inhibitor to Fgl2. Graft rejection of all tissues and organs work by common phenomena – the recipient mounts an immune and inflammatory response to the foreign tissue or organ. Applicant has determined that Fgl2 is an immune coagulant

that is involved in transplant rejection. Applicant should not be limited to a particular type of transplant as the involvement of Fgl2 would be the same in respect of the rejection of any transplant. Further, in the present application, Applicant has provided three distinct examples of how inhibiting Fgl2 can be used to prolong graft survival. In particular, in Example 2(a), Applicant has shown that antibodies to Fgl2 are useful in preventing rejection of a small intestinal allograft. In Example 2(b), Applicant has shown that antibodies to Fgl2 can prevent rejection of a liver xenograft. In Examples 4 and 5, Applicant has shown that antibodies to Fgl2 can prevent fetal loss. We point out that the fetus is a well accepted type of transplant as the maternal and fetal tissues are not identical.

In addition to the data in the application, Applicant has shown that inhibiting Fgl2 can prolong the survival of a heart transplant. In this regard, we are submitting a Declaration under 37 CFR 1.132 executed by inventor Gary Levy which demonstrates that the claimed method works in preventing rejection of a cardiac allograft. In particular, the results presented in the Declaration demonstrate that the mice receiving antibodies to Fgl2 had increased survival of the cardiac allograft as compared to the untreated mice.

Consequently, we respectfully submit that the showing of three examples of transplants in the application along with the data presented in the Declaration would enable one of skill in the art to make and use the invention in any type of transplant.

Applicant also submits that enabling the invention using antibodies to Fgl2 would be sufficient to enable one of skill in the art to use any other inhibitor of Fgl2 in order to practice the invention. Undue experimentation would not be required in order to make and use other inhibitors of Fgl2. For example, Applicant has provided sufficient guidance as to how one can prepare other inhibitors of Fgl2, including antisense molecules, which are described on page 9, line 30 through to page 12, line 8 of the application as filed. Further, inhibitors of Fgl2 are known in the art. For example, Ning et al. (J. of Immunology, 1998, 160: 3487-3493) demonstrate that Ribavirin, a synthetic

guanosine analogue, inhibits the expression of MHV-3-induced mRNA of Fgl2. Marazzi et al. (J. of Immunology, 1998, 161: 138-147), who are interested in the role of Fgl-2 (fibroleukin) in T-lymphocytes, have prepared monoclonal antibodies to peptides from the carboxyl-terminal end of the deduced protein as well as to a recombinant protein fragment expressed in E. coli. These papers demonstrate that one skilled in the art could readily isolate Fgl2 inhibitors that may be useful in the present invention.

With respect to the enablement of the antibodies, Applicant has provided sufficient guidance to enable one of skill in the art in order to prepare antibodies other than the two specific antibodies that were prepared in the specification. In this regard, we refer to page 6, line 26 to page 9, line 29 of the application as filed.

Once one of skill in the art has an Fgl2 inhibitor they can readily test it for its ability to prolong graft survival using models known in the art including the ones described in the application.

In view of the foregoing, we respectfully request that the objections to the claims as lacking enablement be withdrawn.

2. Written Description

The Examiner has also objected to claims 1-4 under 35 USC §112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The invention relates to the realization by the Applicant that inhibiting Fgl2 could be used to prevent and treat transplant rejection. One of skill in the art would readily appreciate that Applicant had possession of the invention at the time the application was filed. The Examiner states that "the written description requirement for a claimed genus may be satisfied through sufficient description of a representation number of species ...". As mentioned above, Applicant has provided three distinct examples in the

application as filed of how inhibiting Fgl2 can be used to prevent and treat graft rejection. The examples include both allograft and xenograft and therefore would be representative of the entire genus of any graft.

With respect to claiming any inhibitor of Fgl2, we point out that Applicant is not attempting to claim Fgl2 inhibitors *per se*, but rather to the use of Fgl2 inhibitors to prevent or treat graft rejection. In making the objection, the Examiner asks Applicant to direct its attention to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. §112 ¶1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001 (hereinafter "the Guidelines"). We respectfully submit that the Examiner is applying the Guidelines in the present case using the principles that were established when examining claims to novel nucleic acid or protein sequences. As the examiner is aware, the Guidelines were prepared as a result of a decision that dealt with whether or not the disclosure of a rat sequence was sufficient written description for a claim that related to the sequence from all vertebrates (*University of California v. Eli Lilly*, CAFC, 43 USPQ 2d 1398, 1997). This case dealt with the claims that related to nucleic acid molecules *per se* and not to uses of the nucleic acids or proteins. In the present case, Applicant is not trying to claim the genus of Fgl2 inhibitors, only to claim the method of prevention and treatment of graft rejection using such inhibitors. In the Guidelines, there is only one example, Example 18, that addresses the case wherein the invention relates to a method where the novelty is in the method steps and not in the nucleic acid molecule. In that case, the example determines that "a single embodiment is representative of the genus".

The application definitely provides a sufficient written description to inform a skilled artisan that Applicant was in possession of the claimed invention as whole at the time the application was filed. The claims under examination are directed to a single embodiment (e.g. treatment of graft rejection by inhibiting Fgl2) and not a genus as the Examiner appears to have concluded. Therefore, the guidelines used for examination of the present claims should be "for each claim drawn to a single embodiment or species" and not "for each claim drawn to a genus" (see the Guidelines, p.1106). Under

this guideline, if the application describes an actual reduction to practice of the claimed invention, it will qualify as fulfilling the written description requirement. It is not necessary to include a description of a representative number of species.

The application provides ample disclosure on page 6-11 on how Fgl2 inhibitors such as antibodies and antisense molecules can be prepared. Further, on page 11-12, it is clearly stated that other substances that inhibit Fgl2 may be isolated and used in the method of invention.

In summary, the disclosure of the application makes it clear that applicant was in possession of the invention, (which relates to a novel method for preventing or treating graft rejection by inhibiting Fgl2), at the time of filing the application. Applicant has provided examples of Fgl2 inhibitors that can be useful in the invention. Applicant is not required to exemplify every possible Fgl2 inhibitor in the application in order to demonstrate that they were in possession of the invention as the invention relates to a novel method for preventing or treating graft rejection and not to novel Fgl2 inhibitors.

In view of the foregoing, we respectfully request that the objections to the claims under 35 USC §112, first paragraph for lacking written description be withdrawn.

Double Patenting

We note the Examiner's comments that claims 1-4 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22-23 and 34 of copending application no. 10/096,255. Applicant will file a Terminal Disclaimer or remove the overlapping claims of the copending application once we receive an indication that the current claims are allowable.

Formal Drawings

We are submitting new Figures 2, 3, 5-7, 8A-B, 9A-B, 10A-B, 11-13, 15, 16, 18 and 19-22 in order to respond to the Notice of Draftperson's Patent Drawing Review. No new matter is contained in the drawings.

The Commissioner is hereby authorized to charge any fee (including any claim fee) which may be required to our Deposit Account No. 02-2095.

Attached hereto is a marked-up version of the changes made to the figures by the current amendment. The attached page is captioned **"Version With Markings To Show Changes Made"**.

In view of the foregoing comments and amendments, we respectfully submit that the application is in order for allowance and early indication to that effect is respectfully requested. Should the Examiner deem it beneficial to discuss the application in greater detail, he is kindly requested to contact the undersigned by telephone at (416) 364-7311 at his convenience.

Respectfully submitted,

Gary Levy

M. Gravelle

Micheline Gravelle
Registration No. 40,261

Bereskin & Parr
Box 401, 40 King Street West
Toronto, Ontario
Canada M5H 3Y2
(416) 364-7311

MG/jl
Encl.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Disclosure:

The paragraph beginning at page 1, line 1 has been amended as follows:

--This application is a divisional of United States Patent Application Serial No. 09/442,143 filed November 15, 1999 (now [pending] U.S. Patent No. 6,403,089), which is a continuation of PCT/CA98/00475, filed May 15, 1998, which claims priority to provisional application 60/061684 filed October 10, 1997 (now abandoned) and provisional applications 60/046,537 filed May 15, 1997 (now abandoned).--

Paragraph beginning at page 5, line 7 has been amended to read as follows:

--Figure 8A shows the nucleotide sequence of the mouse (SEQ.ID.NO.: 10) and human (SEQ.ID.NO.: 11) Fgl2 gene promoter regions;

Figure 8B shows the nucleotide sequence of the mouse (SEQ.ID.NO.: 10) and human (SEQ.ID.NO.: 11) Fgl2 gene promoter regions;--

Paragraph beginning at page 5, line 9 has been amended to read as follows:

--Figure 9A shows the nucleic acid sequence of the transcription binding sites in the putative promoter region of hfgl2 (SEQ.ID.NO.: 12);

Figure 9B shows the nucleic acid sequence of the transcription binding sites in the putative promoter region of hfgl2 (SEQ.ID.NO.: 12);--

In the Figures

Figures 2, 3, 5-9, 10A-B, 11-13, 15, 16, 18 and 19-22 presently of record have been replaced with the enclosed Figures 2, 3, 5-7, 8A-B, 9A-B, 10A-B, 11-13, 15, 16, 18 and 19-22.